Arterial Pulse Pressure and Its Association With Reduced Stroke Volume During Progressive Central Hypovolemia

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Background: **The reduction of stroke volume (SV) during hemorrhage reflects the degree of blood loss, but accurate assessment of SV in bleeding patients in the field currently is not possible. In a previous pilot study, we reported that arterial pulse pressure and estimated sympathetic nerve activity (SNA) in trauma patients who died of hemorrhagic injuries was significantly lower than that observed in patients who did not die. For the current study, we measured mean arterial blood pressure (MAP), pulse pressure (PP), SV, and muscle sympathetic nerve activity (MSNA) in human subjects during progressive lower body negative pressure (LBNP) to test the hypothesis that a reduction in PP tracks the reduction of SV and change in MSNA during graded central hypovolemia in humans.**

Methods: **After a 12-minute baseline data collection period, 13 men were exposed to LBNP at −15 mm Hg for 12 minutes followed by continuous stepwise increments to −30, −45, and −60 mm Hg for 12 minutes each.**

Results: **Comparing baseline to −60 mm Hg chamber decompression, systolic blood pressure (SBP) decreased (from 129 ± 3.0 to 111 ± 6.1 mm Hg; $p = 0.005$) and diastolic pressure was unchanged (78 ± 3.0 versus 81 ± 4.0 mm Hg; $p = 0.55$). Pulse pressure decreased (from 50 ± 2.5 to 29 ± 4.0 mm Hg; $p = 0.0001$). LBNP caused linear reductions in PP and SV (from 125 ± 9.2 to 47 ± 6.4; $r^2 = 0.99$), and increases in MSNA (from 14 ± 3.5 to 36 ± 4.6 bursts/min^{-1}; $r^2 = 0.96$) without a significant change in MAP ($r^2 = 0.28$). PP was inversely correlated with MSNA ($r^2 = 0.88$) and positively correlated with SV ($r^2 = 0.91$).**

Conclusions: **Reduced PP resulting from progressive central hypovolemia is a marker of reductions in SV and elevations in SNA. Therefore, when SBP is >90 mm Hg, PP may allow for early, noninvasive identification of volume loss because of hemorrhage and more accurate and timely triage.**

Key Words: **Blood pressure, Hypovolemia, Stroke volume, Sympathetic nerve activity.**

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Acute uncontrolled hemorrhage, subsequent circulatory collapse, and resulting shock account for about 50% of the deaths on the battlefield[1] and up to 82% of the early operative deaths from trauma in the civilian arena.[2] However, once the trauma patient is delivered to the hospital, hemostasis obtained and resuscitation completed, the mortality rate from hemorrhage drops to between 2% and 4%.[1,2] Therefore, it is likely that the survival rate from severe hemorrhage may be improved, particularly in mass casualty or remote situations, by enhancing the capabilities for early, more accurate diagnosis, improved triage decision support to first level responders, and effective interventions. Combining these advances should result in decreased prehospital and early hospital mortality from hemorrhagic shock.

The vital sign monitors placed in emergency transport vehicles provide the medic with routine measures of arterial systolic, diastolic and mean blood pressures, heart rate, and arterial oxygen carrying capacity (SpO_2) of trauma patients. Abnormalities in these vital signs, particularly in the presence of poor motor scores, can provide medics with excellent decision-support information regarding triage categories, evacuation priority, and required interventions. Unfortunately, such abnormalities are late predictors of poor outcomes because of compensatory mechanisms that buffer against changes in arterial blood pressure and SpO_2.[3] Mortality from hemorrhage could be reduced with identification of other noninvasive hemodynamic measurements that provide early assessment of circulatory shock.

In a recent pilot study,[4] vital sign measurements collected en route to a hospital revealed significantly lower pulse pressures in trauma patients who died from hemorrhagic shock despite no significant differences in systolic, diastolic, and mean arterial pressures compared with those patients who lived. In addition, frequency domain analysis of R-R intervals showed that vital signs that estimate changing sympathetic nerve activity may also provide early information about clinical outcome. These preliminary results suggested that pulse pressure may provide the first responder with an earlier assessment of blood loss than systolic, diastolic or mean pressures. Therefore, we performed continuous measurements of mean arterial blood pressure, pulse pressure, stroke volume, and muscle sympathetic

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nerve activity in human subjects during progressive reduction in central blood volume to test the hypothesis that a reduction in pulse pressure is associated with early changes in physiologic responses associated with blood loss.

PATIENTS AND METHODS

Subjects

Fourteen healthy men with a mean (±SE) age of 40 ± 3 years, height of 177 ± 2 cm, and weight of 80.2 ± 2.7 kg volunteered to participate as subjects for this investigation after all procedures and risks associated with the experiments were explained. Their voluntary written informed consent to participate in the study was obtained. All procedures were reviewed and approved by the human use committee of Brooke Army Medical Center, Fort Sam Houston, TX. All subjects were nonsmokers and normotensive, and their selection into the study was based on results of a detailed medical history to assure absence of cardiovascular disease. Individuals taking prescription drugs were excluded and subjects refrained from taking any medications at the time of the experiments. Because of potential effects on vascular volume and autonomic functions, subjects were asked to refrain from exercise and stimulants such as caffeine and other nonprescription drugs 48 hours before testing.

Experimental Protocol and Analysis

Each subject reported to the laboratory on one occasion and underwent a 60-minute lower body negative pressure (LBNP) protocol consisting of a 12-minute baseline period followed by exposure to −15, −30, −45, and −60 mm Hg decompression for 12 minutes each. LBNP was used as a method to induce central hypovolemia and subsequent hemodynamic and muscle sympathetic nerve activity (MSNA) responses similar to those measured during a steady-state hemorrhage.[5–7] The initial 2 minutes of each 12-minute data collection period was used to allow the subject to reach a steady-state status without data collection.[7] The remaining 10 minutes was required to collect our hemodynamic and MSNA data. Measurements during baseline and each LBNP level included heart rate, stroke volume, arterial blood pressures, and MSNA. Because large, deep breaths (as might occur during a sigh) could confound the interpretation of the effects of LBNP on MSNA[8] and interfere with thoracic impedance measurements, subjects breathed in time to a metronome set at a pace of 15 breaths per minute, and did not deviate from this controlled breathing frequency during the period of data collection. Subjects were instructed not to contract their leg muscles during LBNP. Premature test termination was based on occurrence of any one or a combination of the following: (1) onset of symptoms of cardiovascular collapse such as a fall in systolic blood pressure greater than 15 mm Hg and/or a fall in heart rate greater than 15 beats per minute between adjacent 1-minute measurements; (2) progressive fall in systolic blood pressure below 80 mm Hg; and (3) subject request because of symptoms such as nausea or dizziness. To assure subject safety, an ACLS certified physician was present in the laboratory building during all LBNP tests.

Heart Rate and Blood Pressure

Continuous heart rate (HR) was measured with a Hewlett-Packard monitoring system from a standard electrocardiogram (ECG). A Finapres fingercuff blood pressure monitoring device (Ohmeda Inc., Englewood, Colo.) was placed at heart level to provide a noninvasive measurement of beat-by-beat systolic (SBP) and diastolic (DBP) blood pressure. The ability to obtain Finapres blood pressure recordings was not affected by high levels (i.e. >45 mm Hg) of LBNP. Periodic blood pressure measurements also were conducted with a Colin automated sphygmomanometer to verify the readings obtained from the Finapres. From the Colin sphygmomanometer recordings, mean arterial pressure (MAP) was estimated by dividing the sum of SBP and twice DBP by three, and pulse pressure (PP) was calculated by subtracting DBP from SBP.

Measurement of Stroke Volume

Stroke volume (SV) was measured noninvasively using thoracic electrical bioimpedance (TEB). TEB was measured using four circumferential electrodes, two placed around the base of the neck and two placed around the thorax at the level of and distal to the xiphoid process. A bioelectric impedance cardiograph unit (HIC-2000, Bio-impedance Technology, Inc., Chapel Hill, N.C.) was used to introduce a constant current of 4 mA at 100 KHz frequency across the outer electrodes and detect changes in electrical impedance with each pulse beat across the inner pairs of electrodes.[9] The analog signal of the electrocardiogram wave form (ECG), baseline thoracic impedance (Z_0), and the change in impedance over time (dZ/dt) were converted to a digital signal for analysis using National Instruments LabView software. The R-wave of the ECG was taken as a landmark to average dZ/dt waveforms over 10 cardiac cycles that were recorded at the beginning of minutes 2, 8, and 10 of each baseline and LBNP level. Stroke volume for minutes 2, 8, and 10 were determined as the average SV from the 10 cardiac cycles, and average stroke volume at baseline and each level of LBNP was calculated as the average SV at 2, 8, and 10 minutes. The following algorithm was used to estimate SV from the ECG and impedance:[9]

$$SV = \frac{\rho L^2 T(dZ/dt)}{Z_0^2}$$

Where:

ρ = the average electrical resistivity of blood at 100 KHz (150 ohm-cm).

L = the mean distance between the two inner electrodes in cm.

T = the ventricular ejection time in seconds as measured from the dZ/dt and ECG waveforms.

Estimates of stroke volume using thoracic impedance have been reported with correlation coefficients of 0.70 to 0.93 in comparison with thermodilution techniques under specific clinical conditions.[10] We chose TEB because it provided a noninvasive technique for continuous measurement of SV that tracks the progressive reduction in central blood volume in the LBNP model.[4,5,16,20]

Muscle Sympathetic Nerve Activity

Muscle sympathetic nerve activity (MSNA) was measured directly with a Nerve Traffic Analyzer (Model 662C-1, University of Iowa Bioengineering, IA City, Iowa) according to the procedures described by Cooke.[11] Briefly, multifiber efferent sympathetic nerve traffic from peroneal nerve muscle fascicles at the popliteal fossa was recorded with tungsten microelectrodes (Frederick Haer and Co., Bowdoninham, Maine). The course of the nerve was mapped by stimulating the nerve through the skin with a pencil shaped electrode (10–50 v; 0.1 ms duration). The nerve was located when electrical stimulation produced muscle twitching in the lower leg. Once the nerve was located, two sterile wire electrodes (diameter approximately 0.2 mm) were introduced through the skin to a depth of approximately 0.5 to 1 cm; one electrode served as the ground and the other as the recording electrode. The recording electrode was advanced into the region of the nerve while the operator listened for characteristic insertion "bursts" that would indicate penetration of the nerve fascicle. The electrode was then maneuvered and adjusted so that spontaneous sympathetic bursts were apparent, and the subsequent nerve activity was recorded. Both electrodes were connected to a differential pre-amplifier, and then to an amplifier (total gain 70,000) where the nerve signal was band-pass filtered (700–2000 Hz), and integrated (time constant, 0.1 s) to obtain mean voltage neurograms. Satisfactory recordings of MSNA were defined by spontaneous, pulse synchronous bursts that increased during end-expiratory apnea, and did not change during tactile or auditory stimulation. For later off-line analysis, bursts of MSNA were detected automatically through several criteria. Potential bursts were identified within a 0.5 s search window centered on an expected burst peak latency from preceding R-waves of 1.3 s.[12] Potential bursts were also evaluated based on amplitude, using a signal-to-noise baseline criterion of approximately 3:1.

Statistical Analysis

We calculated regression coefficients between LBNP and MAP, MSNA, SV, and PP and between PP and SV and MSNA. We used repeated measures ANOVA to compare baseline hemodynamics with those at the highest level of LBNP. Significance was set at $p \leq 0.05$. Data are presented as means ± SE unless specified otherwise.

RESULTS

Data from one subject were not analyzable because of technical problems, and so we report hemodynamic results from thirteen subjects. Of these thirteen subjects, we were successful in placement and recording of MSNA from 10 subjects during baseline rest. As a result of fluid accumulation in the lower extremities or mechanical displacement of the recording electrode during LBNP, MSNA was recorded successfully in 9 subjects during 15 mm Hg LBNP, 7 subjects during 30 mm Hg LBNP, 6 subjects during 45 mm Hg LBNP, and 4 subjects during 60 mm Hg LBNP. Such success rates in maintaining adequate nerve recordings during LBNP are not uncommon.[6] Five subjects became presyncopal at and could not complete the −60 mm Hg LBNP stage, so analyses were conducted only on hemodynamic measurements conducted before the onset of presyncopal symptoms. Comparisons between baseline and −60 mm Hg revealed that heart rates increased significantly from 57 ± 3.0 to 87 ± 5.0 bpm ($p = 0.0001$). Systolic pressure decreased from 129 ± 3.0 to 111 ± 6.1 mm Hg ($p = 0.005$). Diastolic pressure was 78 ± 3.0 at baseline and 81 ± 4.0 mm Hg at −60 mm Hg chamber decompression ($p = 0.55$). Pulse pressure decreased from 50 ± 2.5 to 29 ± 4.0 mm Hg ($p = 0.0001$).

Figure 1 shows the relationship between progressive increases in LBNP and mean (±SE) MAP, SV, PP, and MSNA. As a group, LBNP caused linear reductions in PP ($r^2 = 0.94$) and SV ($r^2 = 0.99$) and increases in MSNA ($r^2 = 0.96$) without a significant change in MAP ($r^2 = 0.28$). Figure 2 illustrates that PP was inversely correlated with MSNA ($r^2 = 0.88$) and positively correlated with SV ($r^2 = 0.91$). The relationship between SV and PP appeared to tighten using a third-order rather than simple linear regression ($r^2 = 0.99$) as shown in Figure 3.

DISCUSSION

We measured arterial blood pressures, stroke volume and muscle sympathetic nerve activity in human subjects exposed to progressive LBNP to assess whether reductions in arterial pulse pressure would provide an early predictor of central blood volume loss. A significant volume deficit was reflected by a >60% reduction in SV from baseline to −60 mm Hg LBNP (Fig. 1). Although not measured in this experiment, decreased perfusion has been demonstrated in the LBNP model by dramatic reductions in peripheral blood flow and significant tachycardic responses.[6] The primary new findings are (1) pulse pressure decreases early and in a linear fashion with the magnitude of central hypovolemia with no change in mean arterial pressure; and (2) decreased pulse pressure during central blood volume reduction is correlated significantly with reduced stroke volume and increased sympathetic nerve activity. In concurrence with our most recent analyses from trauma patient data,[4] our results suggest that pulse pressure is an earlier predictor of outcome from blood loss than systolic, diastolic, or mean arterial pressures, and may provide important diagnostic and prognostic information that may assist the first responder in on-site triage, remote triage, and evacuation priority.

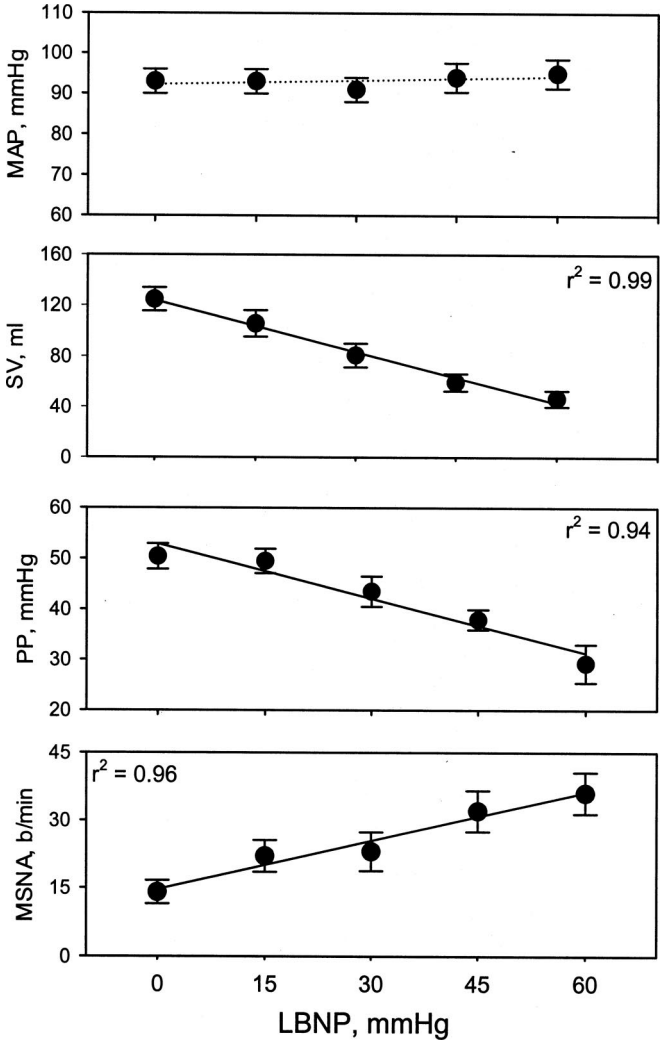

Fig. 1. *Hemodynamic and neural responses to progressive lower body negative pressure (LBNP); MAP, mean arterial pressure; SV, stroke volume; PP, pulse pressure; MSNA, muscle sympathetic neural activity.*

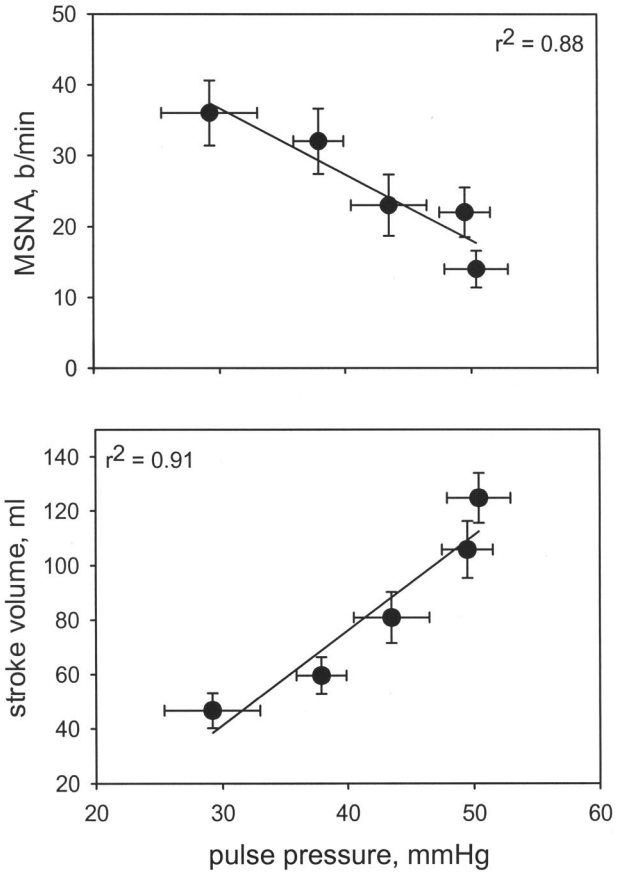

Fig. 2. *Linear associations among muscle sympathetic neural activity (MSNA) and stroke volume plotted as functions of pulse pressure.*

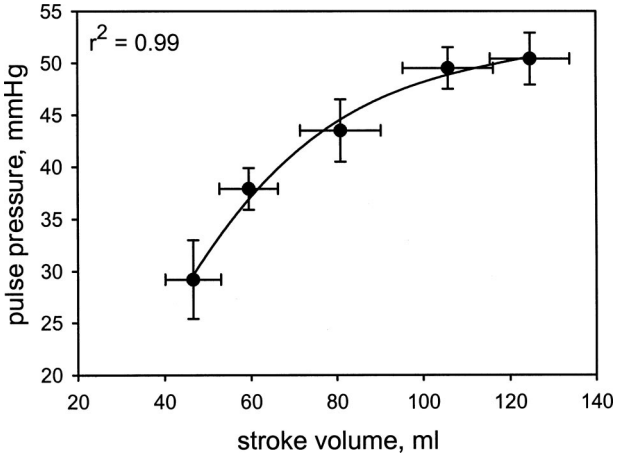

Fig. 3. *Association between stroke volume and pulse pressure modeled with a three-order regression.*

Stroke Volume and Pulse Pressure as a Marker of Hemorrhage

We have proposed the use of LBNP as an experimental tool to simulate central hemodynamic and autonomic responses that occur during hemorrhage in humans.[6] Absolute equivalence between the magnitude of negative pressure applied and the magnitude of actual blood loss cannot at this time be determined. Because afterload (DBP) was not significantly affected from baseline to −60 mm Hg LBNP, the reduction in SV during LBNP resulted from reduced preload. Therefore, the linear relationship reported consistently between reduced stroke volume and increased LBNP[6,13,14] supports the notion that loss of central blood volume and lower cardiac filling is proportional to the magnitude of LBNP. Thus, changes in stroke volume mirror changes in central blood volume. Our observation in the present study that pulse pressure correlates with stroke volume supports the hypothesis that reduced pulse pressure during blood loss may act as an effective (accurate) marker of circulating intravascular volume. However, the central hypovolemia induced with LBNP is different from that of hemorrhage for the primary reason that no actual blood is lost during LBNP. To examine the relationship between actual blood loss, stroke volume, and pulse pressure, Leonetti et al.[15]

withdrew approximately 375 mL of blood from human volunteers over the course of about 6 minutes. Stroke volume and pulse pressure were measured continuously from finger arterial pressure by modeling arterial flow with a nonlinear, three-element model.[16] Both stroke volume ($r^2 = 0.88$; $p < 0.001$) and pulse pressure ($r^2 = 0.64$; $p < 0.001$) correlated directly with volume loss, and the authors proposed that both variables are equally able to predict blood volume reductions in humans.[15]

Lower central blood volume leads to reduced cardiac filling and stroke volume in accordance with the Frank-Starling relationship. With this construct, smaller cardiac chamber size can act as a volume sensor and increase peripheral sympathetic nerve activity through baroreflex-mediated neural transmissions.[17,18] This concept is supported by observations of a linear relationship between reduced stroke volume and elevated MSNA in our LBNP model.[19,20] Because falls in pulse pressure correlated with decreasing stroke volume in the present experiment, it is not surprising that we found pulse pressure to be linearly related with increasing MSNA.

Relationship Between Pulse Pressure and Stroke Volume

For each cardiac cycle, the degree to which elevations in mean arterial pressure generate the arterial pulse pressure is a function of both stroke volume and arterial tone.[21] Michard et al.[22,23] investigated arterial pulse pressure as a predictor of the subsequent increase in stroke volume in response to either the addition of positive end-expiratory pressure in patients with acute lung injury or fluid loading in septic ventilator-dependent patients. In patients with acute respiratory distress syndrome requiring artificial ventilation, the degree of reduction in pulse pressure during a breath was related quantitatively to the subsequent decrease in cardiac output in response to the addition of increasing amounts of airway pressure.[22] Furthermore, in ventilator-dependent patients with severe sepsis, pulse pressure elevation predicted the amount of increase of the cardiac output in response to intravascular fluid loading.[23] Therefore, stroke volume can be represented as the product of pulse pressure and arterial vessel distensibility.[24]

If arterial distensibility remained constant during progressive central blood volume reduction, one would expect changes in pulse pressure to be linearly associated with changes in stroke volume. Chelma et al.[25] measured aortic pressure directly through catheterization and applied the windkessel model to derive total arterial compliance (distensibility), and also estimated arterial compliance with the ratio of stroke volume and pulse pressure in groups of normal controls and cardiac patients ($n = 31$). Stroke volumes in their subjects ranged from 25 to 130 mL, and pulse pressures ranged from 27 to 88 mm Hg. The regression between the two estimates of compliance fell on the line of identity ($r = 0.98$), suggesting that distensibility can be assessed simply with stroke volume and pulse pressure and that it is constant over a wide range of volumes and pressures. In the present study, we described the relationship between pulse pressure as a function of changes in stroke volume (within ranges similar to those reported by Chelma et al.[25]) in the same subjects during LBNP. Although we observed that 91% of the variance in the relationship was represented by a simple linear regression model (Fig. 2), the prediction of pulse pressure by stroke volume was improved to 99% when a three-element regression model was applied (Fig. 3). Our results suggest that arterial distensibility is not constant, but continues to decrease with the progressive reduction in central blood volume in our LBNP model. This is not surprising, given that distensibility was estimated in the study by Chelma et al.[25] in subjects at rest, and the apparent change in distensibility suggested by data presented in Figure 3 was provoked in the same subjects as they were compensating with increases in sympathetic neural activity to progressive central hypovolemia. Based on our recent comparison of physiologic responses to LBNP compared with hemorrhage,[6] our data suggest that distensibility decreased rapidly during the initial 400 to 550 mL of central blood loss (10–20 mm Hg LBNP) followed by a constant distensibility during central volume reduction between 500 to 1000 mL (20–40 mm Hg LBNP). The marked vasoconstriction that accompanies central blood volume reduction >1000 mL (>40 mm Hg LBNP) significantly reduces vessel distensibility so that large reductions in pulse pressure translate to disproportionately smaller reductions in stroke volume (Fig. 3).

Arterial distensibility can be affected by sympathetic activation of vasoconstriction (arterial resistance), and inherent elastic properties (compliance) of the vessel walls. The initial steep drop in pulse pressure and stroke volume represents a sympathetically mediated vasoconstriction in vessels that are relatively filled with adequate blood when the vessels are at their highest compliance. With further volume loss, vessel compliance is reduced and remains constant over a range of blood loss indicating that vessel distensibility remained constant. When maximal vasoconstrictor capacity is reached,[13] distensibility is reduced maximally despite further sympathetic activation.

Limitations

We acknowledge that LBNP differs significantly from traumatic hemorrhage in two primary characteristics. First, central blood volume is reduced with LBNP by fluid redistribution and accumulation in the lower extremities rather than loss of blood from the circulation. However, we have presented evidence that hemodynamic and autonomic responses induced by LBNP are similar to those produced by actual blood loss.[6] Therefore, data from several laboratories[6] suggest that changes in SV and PP are induced by alterations in central hemodynamics and should not be affected by artifactual fluid accumulation in the peripheral circulation. Second, LBNP does not introduce tissue injury and pain associated with trauma. In the present study, HR and SBP had high correlations with SV during the progressive LBNP ($r^2 = 0.82$ and 0.89, respectively). These tight relationships most likely reflect a strength of the LBNP model that isolates hemodynamic effects of central blood volume reduction from the variable effects introduced by injury and pain that are present in the

trauma patient. Thus, injury and pain can introduce significant variability to SBP and HR responses through important influences on sympathetic activation. Therefore, it is likely that severe injury and pain may mask the predictability of patient outcome based on HR and SBP response of hemodynamics alone. Consequently, the high variability of HR and SBP responses to actual trauma because of the added impact of injury and pain may explain the lack of specificity of these markers as early predictors of patient outcome.[4] Because increased sympathetic activation of vasoconstriction can reduce arterial distensibility, we cannot dismiss the possibility that injury and pain in addition to central blood loss in trauma could influence the interpretation of reductions in PP in multiple trauma patients. However, recent results obtained from prehospital vital signs in trauma patients with injury and pain demonstrated that PP was significantly lower in patients who died while their SBP, DBP, MAP, HR, and SpO_2 were similar to the cohort of patients who lived.[4] Therefore, prehospital data obtained from trauma patients are consistent with the results of the present investigation that PP may represent an early marker of blood loss and stroke volume independent of the presence of injury and pain.

CONCLUSIONS

A trauma patient presenting with a systolic blood pressure of 90 mm Hg usually requires rapid diagnosis and intervention.[26] Bleeding patients with blood pressures >90 mm Hg (as simulated in the present study) could be progressing quickly toward cardiovascular collapse and shock because blood pressure before cardiovascular collapse does not accurately track blood loss. Stroke volume reflects central volume directly, but stroke volume cannot be obtained easily by a first responder or early in the emergency department. We present evidence in the current report that pulse pressure could be considered as a surrogate for stroke volume and subsequently as a means to track loss of blood volume in trauma patients. Monitoring of pulse pressure could be an easily obtained surrogate of stroke volume, essentially an early warning measure, alerting medical personnel that casualties appearing stable, may in fact be approaching cardiovascular collapse. These noninvasive easily acquired data may be even more useful as a triage tool in a mass casualty situation where effective triage decisions depend on accurate prioritization.

REFERENCES

1. Bellamy RF. The causes of death in conventional land warfare: implications for combat casualty care research. *Mil Med.* 1984;149:55–62.
2. Carrico CJ, Holcomb JB, Chaudry IH, PULSE trauma work group. Post resuscitative and initial utility of life saving efforts. Scientific priorities and strategic planning for resuscitation research and life saving therapy following traumatic injury: report of the PULSE trauma work group. *Acad Emerg Med.* 2002;9:621–626.
3. Orlinsky M, Shoemaker W, Reis ED, Kerstein MD. Current controversies in shock and resuscitation. *Surg Clin North Am.* 2001;81:1217–1262.
4. Cooke WH, Salinas J, Convertino VA, et al. Heart rate variability and its association with mortality in pre-hospital trauma patients. *J Trauma.* 2006;60:363–70; discussion 370.
5. Convertino VA. Lower body negative pressure as a tool for research in aerospace medicine and military medicine. *J Gravit Physiol.* 2001;8:1–14.
6. Cooke WH, Ryan KL, Convertino VA. Lower body negative pressure as a model to study progression to acute hemorrhagic shock in humans. *J Appl Physiol.* 2004;96:1249–1261.
7. Levine BD, Giller CA, Lane LD, Buckey JC, Blomqvist CG. Cerebral versus systemic hemodynamics during graded orthostatic stress in humans. *Circulation.* 1994;90:298–306.
8. Eckberg DL, Nerhed C, Wallin BG. Respiratory modulation of muscle sympathetic and vagal cardiac outflow in man. *J Physiol.* 1985; 365:181–196.
9. Kubicek WG, Karnegis JN, Patterson RP, Wilsoe DA, Mattson RH. Development and evaluation of an impedance cardiac output system. *Aerospace Med.* 1966;37:1212.
10. Newman DG, Callister R. The non-invasive assessment of stroke volume and cardiac output by impedance cardiography: a review. *Aviat Space Environ Med.* 1999;70:780–789.
11. Cooke WH. Topical anesthetic before microneurography decreases pain without affecting sympathetic traffic. *Autonomic Neurosci Basic Clin.* 2000;86:120–126.
12. Fagius J, Sundlof G, Wallin BG. Variation of sympathetic reflex latency in man. *J Autonom Nerv Syst.* 1987;21:157–165.
13. Convertino VA. G-factor as a tool in basic research: mechanisms of orthostatic tolerance. *J Gravit Physiol.* 1999;6:P73–P76.
14. Convertino VA, Holcomb JB. Advanced diagnostics for the combat medic. *AMEDD J.* 2003;PB 8-03-7/8/9:42–48.
15. Leonetti P, Audat F, Girard A, Laude D, Lefrere F, Elghozi JL. Stroke volume monitored by modeling flow from finger arterial pressure waves mirrors blood volume withdrawn by phlebotomy. *Clin Auton Res.* 2004;14:176–181.
16. Wesseling KH, Jansen JR, Settels JJ, Schreuder JJ. Computation of aortic flow from pressure in humans using a nonlinear, three-element model. *J Appl Physiol.* 1993;74:2566–2573.
17. Charkoudian N, Martin EA, Dinenno FA, Eisenach JH, Dietz NM, Joyner MJ. Influence of increased central venous pressure on baroreflex control of sympathetic activity in humans. *Am J Physiol Heart Circ Physiol.* 2004;287:H1658–H1662.
18. Bishop VS, Hasser EM. Arterial and cardiopulmonary reflexes in the regulation of the neurohumoral drive to the circulation. *Fed Proc.* 1985;44:2377–2381.
19. Cooke WH, Convertino VA. Association between vasovagal hypotension and low sympathetic neural activity during presyncope. *Clin Auton Res.* 2002;12:483–486.
20. Convertino VA, Ludwig DA, Cooke WH. Stroke volume and sympathetic responses to lower-body negative pressure reveal new insight into circulatory shock in humans. *Auton Neurosci.* 2004;111:127–134.
21. Sunagawa K, Maughan WL, Burkhoff D, Sagawa K. Left ventricular interaction with arterial load studied in the isolated canine ventricle. *Am J Physiol.* 1983;245:H773–H780.
22. Michard F, Chemla D, Richard C, et al. Clinical use of respiratory changes in arterial pulse pressure to monitor the hemodynamic effects of PEEP. *Am J Respir Crit Care Med.* 1999;159:935–939.
23. Michard F, Boussat S, Chemla D, et al. Relation between respiratory changes in arterial pulse pressure and fluid responsiveness in septic patients with acute circulatory failure. *Am J Respir Crit Care Med.* 2000;162:134–138.
24. Burton AC. The pulse and its interpretation. *Physiology and Biophysics of the Circulation.* Chicago: Year Book Medical Publishers; 1972; 160–166.
25. Chelma D, Herbert J-L, Coirault C, et al. Total arterial compliance estimated by stroke volume-to-aortic pulse pressure ratio in humans. *Am J Physiol.* 1998;274:H500–H505.
26. Franklin GA, Boaz PW, Spain DA, Lukan JK, Carrillo EH, Richardson JD. Prehospital hypotension as a valid indicator of trauma team activation. *J Trauma.* 2000;48:1034–1039.